HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use Metaxalone Tablets safely and effectively. See full prescribing information for Metaxalone Tablets

Metaxalone Tablets for oral use
Initial U.S. Approval: 1962

RECENT MAJOR CHANGES

None.

INDICATIONS AND USAGE

Metaxalone Tablets are indicated as an adjunct to rest, physical therapy, and other measures for the relief of discomforts associated with acute, painful musculoskeletal conditions. (1)

DOSAGE AND ADMINISTRATION

The recommended dose for adults and children over 12 years of age is one 640 mg tablet three to four times a day. (2)

DOSAGE FORMS AND STRENGTHS

Tablets: 640 mg. (3)

CONTRAINDICATIONS

- Known tendency to drug induced, hemolytic, or other anemias. (4)
- Patients with severely impaired renal or hepatic function. (4)

WARNINGS AND PRECAUTIONS

- Central Nervous System (CNS) Depression: Metaxalone Tablets may impair mental and/or physical abilities required for the performance of hazardous tasks, such as operating machinery or driving a motor vehicle, and may enhance the effects of alcohol and other CNS depressants. (5.1)
- Hepatic and Renal Impairment: Metaxalone Tablets should be administered with caution to patients with mild to moderate hepatic and renal impairment (5.2)

ADVERSE REACTIONS

The most common adverse reactions to Metaxalone Tablets include drowsiness, dizziness, headache, and nervousness or "irritability", nausea, vomiting, gastrointestinal upset. (6)

To report SUSPECTED ADVERSE REACTIONS, contact CorePharma, LLC at 1-800-850-2719 and www.corepharma.com or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.

DRUG INTERACTIONS

CNS depressants: Use with caution. The sedative effects of Metaxalone Tablets and other CNS depressants (e.g., alcohol, benzodiazepines, opioids, tricyclic antidepressants) may be additive. (7.1)

See 17 for PATIENT COUNSELING INFORMATION

Revised: June/2015

FULL PRESCRIBING INFORMATION: CONTENTS*

***Sections or subsections omitted from the full prescribing information are not listed**

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Metaxalone Tablets are indicated as an adjunct to rest, physical therapy, and other measures for the relief of discomforts associated with acute, painful musculoskeletal conditions.

2 DOSAGE AND ADMINISTRATION

The recommended dose for adults and children over 12 years of age is one Metaxalone Tablet three to four times a day.

3 DOSAGE FORMS AND STRENGTHS

Metaxalone Tablet is available as a 640 mg oval, peach-colored tablet, debossed on one side with **cor 324** and plain on the other side.

4 CONTRAINDICATIONS

The use of Metaxalone Tablets is contraindicated in the following conditions:

- Known tendency to drug induced, hemolytic, or other anemias.
- Patients with severely impaired renal or hepatic function.

5 WARNINGS AND PRECAUTIONS

5.1 Central Nervous System (CNS) Depression

Metaxalone Tablets may enhance the effects of alcohol and other CNS depressants (e.g., benzodiazepines, opioids, tricyclic antidepressants) and may impair mental and/or physical abilities required for performance of hazardous tasks, such as operating machinery or driving a motor vehicle, especially when used with alcohol or other CNS depressants. Therefore, Metaxalone Tablets should be used with caution in patients who take one or more of these CNS depressants. *[See Drug Interactions (7.1)]* Elderly patients may be especially susceptible to CNS effects.

5.2 Hepatic and Renal Impairment Patients

Metaxalone Tablets are metabolized by the liver and excreted in the urine. Use caution when administering Metaxalone Tablets in patients with mild to moderate hepatic or renal impairment. Consider monitoring of liver and renal function in these patients. Metaxalone Tablets are contraindicated in patients with severe hepatic or renal impairment *[See Contraindications (4) and Use in Specific Populations (8.6, 8.7)]*.

6 ADVERSE REACTIONS

The most frequent reactions to Metaxalone Tablets include:
CNS: drowsiness, dizziness, headache, and nervousness or “irritability”;
Digestive: nausea, vomiting, gastrointestinal upset.
Other adverse reactions are:
Immune System: hypersensitivity reaction, rash with or without pruritus;

Hematologic: leucopenia; hemolytic anemia;
Hepatobiliary: jaundice.
Anaphylactoid reactions have been reported with metaxalone.

7 DRUG INTERACTIONS

7.1 Alcohol and CNS Depressants

The sedative effects of Metaxalone Tablets and other CNS depressants (e.g., alcohol, benzodiazepines, opioids, tricyclic antidepressants) may be additive. Therefore, caution should be exercised with patients who take more than one of these CNS depressants simultaneously.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category B. Reproduction studies in rats have not revealed evidence of impaired fertility or harm to the fetus due to metaxalone. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

8.3 Nursing Mothers

It is not known whether this drug is secreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Metaxalone Tablets are administered to a nursing woman.

8.4 Pediatric Use

Safety and effectiveness in children 12 years of age and below have not been established.

8.5 Geriatric Use

The effects of age on the pharmacokinetics of Metaxalone Tablets have not been evaluated.

8.6 Hepatic Impairment

Formal pharmacokinetic studies using Metaxalone Tablets have not been conducted in patients with hepatic impairment. Since metaxalone undergoes hepatic metabolism, Metaxalone Tablets should be used with caution in patients with mild to moderate hepatic impairment. Metaxalone Tablets are contraindicated in patients with severe hepatic impairment. *[See Contraindications (4) and Warnings and Precautions (5.2)]*

8.7 Renal Impairment

Formal pharmacokinetic studies using Metaxalone Tablets have not been conducted in patients with renal impairment. Since metaxalone is excreted in the urine as unidentified metabolites, Metaxalone Tablets should be used with caution in patients with mild to moderate renal impairment. Metaxalone Tablets are contraindicated in patients with severe renal impairment. *[See Contraindications (4) and Warnings and Precautions (5.2)]*

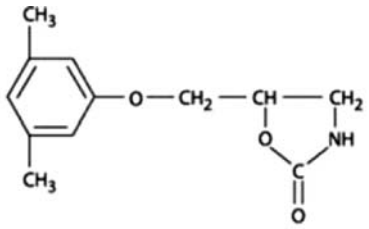
10 OVERDOSAGE

Deaths by deliberate or accidental overdose have occurred with metaxalone, particularly in combination with antidepressants, and have been reported with this class of drug in combination with alcohol.
Treatment – Gastric lavage and supportive therapy. Consultation with a regional poison control center is recommended.

11 DESCRIPTION

Metaxalone Tablet is available as a 640 mg oval, peach-colored tablet, debossed on one side with **cor 324** and plain on the other side. The tablets are for oral administration. Each tablet contains 640 mg metaxalone and the following inactive ingredients: alginic acid, FD&C yellow #6, lactose monohydrate, magnesium stearate, propylene glycol alginate and povidone.

Chemically, metaxalone is 5-[(3, 5- dimethylphenoxy) methyl]-2-oxazolidinone. The empirical formula is $C_{12}H_{15}NO_3$, which corresponds to a molecular weight of 221.25. The structural formula is:



Metaxalone is a white to almost white, odorless crystalline powder freely soluble in chloroform, soluble in methanol and in 96% ethanol, but practically insoluble in ether or water.

12. CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The mechanism of action of metaxalone in humans has not been established, but may be due to general central nervous system depression. Metaxalone has no direct action on the contractile mechanism of striated muscle, the motor end plate, or the nerve fiber.

12.3 Pharmacokinetics

Absorption

In a relative bioavailability study in healthy adult volunteers, the C_{max} (peak plasma concentration) and AUC (extent of absorption) values of metaxalone from Metaxalone Tablets, 640 mg were found to be similar to those from Skelaxin® 800 mg tablets. After a single dose of Metaxalone Tablets, 640 mg, under fasted conditions, mean C_{max} and AUC values were 2 mcg/mL and 16 mcg.h/mL, respectively. The time-to-peak plasma concentration (T_{max}) occurred at 3 h (range 1.5-12h).
Effect of Food
Compared to fasted condition, the presence of a high fat meal resulted in 23% increase in C_{max} with no change in AUC, and a T_{max} of 8h (range 3.5-24h).

Distribution

Although plasma protein binding and absolute bioavailability of metaxalone are not known, the apparent volume of distribution (V/F ~ 800 L) and lipophilicity (log P = 2.42) of metaxalone suggest that the drug is extensively distributed in the tissues.

Metabolism
Metaxalone is metabolized by the liver and excreted in the urine as unidentified metabolites. Hepatic Cytochrome P450 enzymes play a role in the metabolism of metaxalone. Specifically, CYP1A2, CYP2D6, CYP2E1, and CYP3A4 and, to a lesser extent, CYP2C8, CYP2C9, AND CYP2C19 appear to metabolize metaxalone.

Metaxalone does not significantly inhibit major CYP enzymes such as CYP1A2, CYP2A6, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP2E1, and CYP3A4. Metaxalone does not significantly induce major CYP enzymes such as CYP1A2, CYP2B6, and CYP3A4 *in vitro*.

Elimination
The plasma half-life in adult healthy subjects was about 5 hours after administration of Metaxalone Tablets.

Special Populations
Age: The effects of age on the pharmacokinetics of Metaxalone Tablets have not been evaluated.

Gender: Females exhibited higher systemic exposure compared to males following administration of Metaxalone Tablets under fasted state in healthy volunteers. The C_{max} and AUC were both found to be about 40% greater in females compared to males.

13. NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

The carcinogenic potential of Metaxalone Tablets has not been determined.

14 CLINICAL STUDIES

Efficacy studies were not conducted with Metaxalone Tablets. The efficacy of Metaxalone Tablets, 640 mg is based on demonstration of similar systemic exposures to the reference drug, Skelaxin® 800 mg tablets [see *Clinical Pharmacology (12.3)]*.

16 HOW SUPPLIED/STORAGE AND HANDLING

Metaxalone Tablets, 640 mg are available as oval, peach-colored tablet, debossed on one side with **cor 324** and plain on the other side. It is packaged as:

Bottle of 100 tablets, NDC 64720-324-10

Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature].

17 PATIENT COUNSELING INFORMATION

Advise patients that Metaxalone Tablets may impair mental and/or physical abilities required for performance of hazardous tasks, such as operating machinery or driving a motor vehicle, especially when used with alcohol and other CNS depressants. Elderly patients may be especially susceptible to CNS effects.

LB # 717

Manufactured and Distributed by:
CorePharma, LLC
Middlesex, NJ 08846